Barb only please

75925

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jennifer C. Jones Examiner #: 71299 Date: 12/18/02
Art Unit: 1614 Phone Number 308-4624 Serial Number: 09/700,147
Mail Box and Bldg/Room Location: 2007, CM1 Results Format Preferred (circle): PAPER DISK E-MAIL
2001, CM2

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: see attached sheet

Inventors (please provide full names): _____

Earliest Priority Filing Date: 25 MAY 1999

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search claim 24 part (A) only.

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: Barb	NA Sequence (#)		STN	CAS
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	Bibliographic	X	Dr.Link	
Date Completed: 9-18-03	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 30	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 45	Other		Other (specify)	

PTO-1590 (1-2000)

```
=> fil reg; d ide l5
FILE 'REGISTRY' ENTERED AT 13:07:35 ON 18 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   17 SEP 2002  HIGHEST RN 452274-20-3
DICTIONARY FILE UPDATES:  17 SEP 2002  HIGHEST RN 452274-20-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   9004-61-9  REGISTRY
CN   Hyaluronic acid (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   ACP
CN   ACP (polysaccharide)
CN   ACP gel
CN   Durolane
CN   Hyaluronan
CN   Hylartil
CN   Luronit
CN   Mucoitin
CN   Sepracoat
CN   Synvisc
DR   9039-38-7, 37243-73-5, 29382-75-0
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration, Polyester, Polyester formed
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGU,
       DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            8823 REFERENCES IN FILE CA (1967 TO DATE)
             662 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            8837 REFERENCES IN FILE CAPLUS (1967 TO DATE)
```

```
=> fil capl; d que l29; d que l73
FILE 'CAPLUS' ENTERED AT 13:48:08 ON 18 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 18 Sep 2002  VOL 137 ISS 12
FILE LAST UPDATED: 17 Sep 2002  (20020917/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.


L5             1 SEA FILE=REGISTRY ABB=ON  9004-61-9
L6           665 SEA FILE=CAPLUS ABB=ON  L5/D OR L5/DP
L7            76 SEA FILE=CAPLUS ABB=ON  L6(L)ESTER?
L8          8402 SEA FILE=CAPLUS ABB=ON  BIOLOGICAL MATERIALS/CT OR BIOMATERIAL?
                 /OBI
L9         23295 SEA FILE=CAPLUS ABB=ON  MEDICAL GOODS+OLD/CT
L10        22636 SEA FILE=CAPLUS ABB=ON  "PROSTHETIC MATERIALS AND PROSTHETICS"/
                 CT
L24          134 SEA FILE=REGISTRY ABB=ON  HYALURONIC ACID(S)ESTER
L26          229 SEA FILE=CAPLUS ABB=ON  L24
L27           82 SEA FILE=CAPLUS ABB=ON  (L7 OR L26) AND (L8 OR L9 OR L10)
L28       141483 SEA FILE=CAPLUS ABB=ON  REGENERAT?
L29            5 SEA FILE=CAPLUS ABB=ON  L27 AND L28



L5             1 SEA FILE=REGISTRY ABB=ON  9004-61-9
L6           665 SEA FILE=CAPLUS ABB=ON  L5/D OR L5/DP
L7            76 SEA FILE=CAPLUS ABB=ON  L6(L)ESTER?
L8          8402 SEA FILE=CAPLUS ABB=ON  BIOLOGICAL MATERIALS/CT OR BIOMATERIAL?
                 /OBI
L9         23295 SEA FILE=CAPLUS ABB=ON  MEDICAL GOODS+OLD/CT
L10        22636 SEA FILE=CAPLUS ABB=ON  "PROSTHETIC MATERIALS AND PROSTHETICS"/
                 CT
L24          134 SEA FILE=REGISTRY ABB=ON  HYALURONIC ACID(S)ESTER
L26          229 SEA FILE=CAPLUS ABB=ON  L24
L27           82 SEA FILE=CAPLUS ABB=ON  (L7 OR L26) AND (L8 OR L9 OR L10)
L30       333557 SEA FILE=CAPLUS ABB=ON  VIVO
L31            9 SEA FILE=CAPLUS ABB=ON  L27 AND L30
L36          135 SEA FILE=CAPLUS ABB=ON  (L7 OR L26)(L)THU/RL - Role - Therapeutic use
L37           60 SEA FILE=CAPLUS ABB=ON  L36 AND L27
L39        22195 SEA FILE=CAPLUS ABB=ON  (SURGERY OR SURGICAL?)/OBI
L40           11 SEA FILE=CAPLUS ABB=ON  L37 AND L39
```

```
L41      584676 SEA FILE=CAPLUS ABB=ON  FIBRE# OR FIBER# OR MICROFIB?
L42      115967 SEA FILE=CAPLUS ABB=ON  (THREE OR 3)(W)DIMENSION?
L43           7 SEA FILE=CAPLUS ABB=ON  L27 AND L42
L44          14 SEA FILE=CAPLUS ABB=ON  L27 AND L41
L73           9 SEA FILE=CAPLUS ABB=ON  (L31 AND (L40 OR L43 OR L44)) OR (L40
                AND (L43 OR L44)) OR (L43 AND L44)


=> s l29 or l73

L74          14 L29 OR L73

=> fil medl; d que l50; d que l53

FILE 'MEDLINE' ENTERED AT 13:48:11 ON 18 SEP 2002

 FILE LAST UPDATED: 17 SEP 2002 (20020917/UP).  FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary.  Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


L47         6983 SEA FILE=MEDLINE ABB=ON  HYALURONIC ACID/CT
L48         9924 SEA FILE=MEDLINE ABB=ON  ESTERIFICATION/CT OR ESTERS/CT
L49        92701 SEA FILE=MEDLINE ABB=ON  REGENERATION+NT/CT
L50            2 SEA FILE=MEDLINE ABB=ON  L47 AND L48 AND L49



L47         6983 SEA FILE=MEDLINE ABB=ON  HYALURONIC ACID/CT
L48         9924 SEA FILE=MEDLINE ABB=ON  ESTERIFICATION/CT OR ESTERS/CT
L51        21521 SEA FILE=MEDLINE ABB=ON  BIOCOMPATIBLE MATERIALS+NT/CT
L53            5 SEA FILE=MEDLINE ABB=ON  L47 AND L48 AND L51


=> s l50 or l53

L75            6 L50 OR L53

=> fil embase; d que l67; d que l69

FILE 'EMBASE' ENTERED AT 13:48:13 ON 18 SEP 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

 FILE COVERS 1974 TO 13 Sep 2002 (20020913/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L56            4 SEA FILE=EMBASE ABB=ON  HYALURONIC ACID ESTER/CT OR HYALURONIC
                 ACID METHYL ESTER/CT
L61        68224 SEA FILE=EMBASE ABB=ON  REGENERATION+NT/CT
L62         5143 SEA FILE=EMBASE ABB=ON  BIOMATERIAL/CT
L63        64334 SEA FILE=EMBASE ABB=ON  "BIOMEDICAL AND DENTAL MATERIALS"+NT/CT
```

```
L65        8762 SEA FILE=EMBASE ABB=ON  IMPLANT/CT
L66           4 SEA FILE=EMBASE ABB=ON  HYALURONIC ACID ETHYL ESTER/CT OR
                HYALURONIC ACID BENZYL ESTER/CT
L67           1 SEA FILE=EMBASE ABB=ON  (L56 OR L66) AND (L65 OR (L61 OR L62
                OR L63))



L57        7193 SEA FILE=EMBASE ABB=ON  HYALURONIC ACID/CT
L58         172 SEA FILE=EMBASE ABB=ON  HYALURONIC ACID DERIVATIVE/CT
L59        2726 SEA FILE=EMBASE ABB=ON  ESTER/CT
L60        3289 SEA FILE=EMBASE ABB=ON  ESTERIFICATION/CT
L61       68224 SEA FILE=EMBASE ABB=ON  REGENERATION+NT/CT
L62        5143 SEA FILE=EMBASE ABB=ON  BIOMATERIAL/CT
L63       64334 SEA FILE=EMBASE ABB=ON  "BIOMEDICAL AND DENTAL MATERIALS"+NT/CT

L65        8762 SEA FILE=EMBASE ABB=ON  IMPLANT/CT
L69           6 SEA FILE=EMBASE ABB=ON  (L57 OR L58) AND (L59 OR L60) AND
                ((L61 OR L62 OR L63) OR L65)


=> s l67 or l69

L76           7 L67 OR L69

=> fil wpids; d que l72

FILE 'WPIDS' ENTERED AT 13:48:17 ON 18 SEP 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

FILE LAST UPDATED: 16 SEP 2002              <20020916/UP>
MOST RECENT DERWENT UPDATE            200259   <200259/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L70          65 SEA FILE=WPIDS ABB=ON  HYALURONIC ACID#(3A)ESTER?
L71       80394 SEA FILE=WPIDS ABB=ON  REGENERAT?
L72          12 SEA FILE=WPIDS ABB=ON  L70 AND L71


=> dup rem l75,l74,l76,l72
FILE 'MEDLINE' ENTERED AT 13:48:38 ON 18 SEP 2002

FILE 'CAPLUS' ENTERED AT 13:48:38 ON 18 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)
```

FILE 'EMBASE' ENTERED AT 13:48:38 ON 18 SEP 2002

FILE 'WPIDS' ENTERED AT 13:48:38 ON 18 SEP 2002

PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L74
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L72
L77 36 DUP REM L75 L74 L76 L72 (3 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE MEDLINE
ANSWERS '7-20' FROM FILE CAPLUS
ANSWERS '21-25' FROM FILE EMBASE
ANSWERS '26-36' FROM FILE WPIDS

=> d ibib ab hitrn 1-36; fil hom

L77 ANSWER 1 OF 36 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999098521 MEDLINE
DOCUMENT NUMBER: 99098521 PubMed ID: 9884052
TITLE: Semisynthetic resorbable materials from hyaluronan esterification.
AUTHOR: Campoccia D; Doherty P; Radice M; Brun P; Abatangelo G; Williams D F
CORPORATE SOURCE: Fidia Advanced Biopolymers, Albano Terme (PD), Italy.
SOURCE: BIOMATERIALS, (1998 Dec) 19 (23) 2101-27. Ref: 174
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990401

AB In recent years, research on new, biocompatible, degradable materials has seen the development of a series of modified natural polymers. Among these, a new class of materials consisting of different hyaluronan derivatives promises to be useful in a whole range of clinical applications thanks to their varied biological properties. These new materials are obtained by chemical modification of purified hyaluronan consisting of the partial or total esterification of the carboxyl groups of this natural polymer. This review on the properties of the new materials reports some of their biocompatibility and characterization aspects based on findings from studies conducted on the ethyl and benzyl hyaluronan esters, two representative members of this new class of compounds, and is intended to arouse interest in the potential of other, as yet unexplored derivatives. From the results of a number of investigations, the various derivatives appear to possess different physico-chemical properties, especially as far as the degree of hydration and polymer stability are concerned. In addition, the type of esterification and extent of chemical esterification of hyaluronan considerably affects the biological properties of these materials, offering a range of polymers either favouring or, conversely, inhibiting the adhesion of certain types of cell.

L77 ANSWER 2 OF 36 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 94339266 MEDLINE
DOCUMENT NUMBER: 94339266 PubMed ID: 8061127
TITLE: Biodegradation of hyaluronic acid derivatives by

hyaluronidase.
AUTHOR: Zhong S P; Campoccia D; Doherty P J; Williams R L; Benedetti L; Williams D F
CORPORATE SOURCE: Department of Clinical Engineering, University of Liverpool, UK.
SOURCE: BIOMATERIALS, (1994 Apr) 15 (5) 359-65.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941005
Last Updated on STN: 19980206
Entered Medline: 19940922

AB Hyaluronic acid (salt) (HA) has been chemically modified as a biomaterial for medical applications such as controlled drug release matrices, nerve guides and wound dressings. A series of HA derivatives, which include different ester types and different degrees of esterification, have been used to investigate the stability of these materials in testicular hyaluronidase. Gel permeation chromatography and capillary viscometer have been employed to determine the size of the molecules, the former used for the water insoluble derivatives that dissolve in dimethyl sulphoxide, the latter for the water soluble samples. The preliminary experimental results indicated that the molecular weight of fully esterified hyaluronic acid (both ethyl and benzyl esters) did not decrease after treatment in the enzyme for 7 and 14 days while the water soluble partially esterified HA were degraded by the enzyme producing a sharp reduction of viscosity within minutes. These observations tend to suggest that the carboxylic groups in the beta-glucoronic acid unit are the activation centre of this enzyme and the total blockage of these groups can restrict the cleavage of beta (1-->4) glycoside bonds by this enzyme.

L77 ANSWER 3 OF 36 MEDLINE
ACCESSION NUMBER: 2001293641 MEDLINE
DOCUMENT NUMBER: 21244332 PubMed ID: 11346429
TITLE: Evaluation of esterified hyaluronic acid as middle ear-packing material.
AUTHOR: Li G; Feghali J G; Dinces E; McElveen J; van de Water T R
CORPORATE SOURCE: Department of Otolaryngology, Albert Einstein College of Medicine, Bronx, NY 10461, USA.
SOURCE: ARCHIVES OF OTOLARYNGOLOGY -- HEAD AND NECK SURGERY, (2001 May) 127 (5) 534-9.
Journal code: 8603209. ISSN: 0886-4470.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010604
Last Updated on STN: 20010604
Entered Medline: 20010531

AB OBJECTIVE: To evaluate the efficacy of esterified hyaluronic acid (MeroGel) as a middle ear (ME)-packing material. DESIGN: Randomized controlled trial. MATERIAL: Twenty-four guinea pigs. INTERVENTION: Group 1, MeroGel-treated animals (n = 10), bilateral wounding of ME mucosa with 5 of the animals receiving the MeroGel packing in the left ME and 5 of the animals receiving MeroGel in the right ME; group 2, absorbable gelatin sponge-treated animals (n = 10), with the same experimental protocol as in group 1 except that the absorbable gelatin sponge was the packing material; group 3, untreated animals (n = 4), unilateral wounding of the left ME mucosa in 2 animals and in 2 animals in the right ME, with no packing material. Auditory brainstem recordings were performed for all

groups before the ME operation and 5 days and 6 weeks after the operation. RESULTS: Auditory brainstem response recordings at postoperative day 5 showed that all ears with ME packing had hearing losses in the frequency range of 500 to 4000 Hz. The recovery of hearing acuity at postoperative week 6 was significantly better in group 1 (MeroGel-treated) guinea pigs compared with group 2 (the absorbable gelatin sponge-treated) animals. In group 2 animals, 20% of the packing material remained in the ME cavities and new bone formation was observed, while in group 1 animals, there was less packing material in the ME and no formation of new bone. CONCLUSIONS: MeroGel is a nonototoxic packing material with a high level of biocompatibility for ME mucosa; it is an effective supportive material following ME surgery and is easily expelled from the ME cavity.

L77 ANSWER 4 OF 36 MEDLINE
ACCESSION NUMBER: 2002217896 MEDLINE
DOCUMENT NUMBER: 21952091 PubMed ID: 11954459
TITLE: Promoting healing in static wounds.
AUTHOR: Ballard K; Baxter H
CORPORATE SOURCE: Guy's Hospital, London.
SOURCE: NURSING TIMES, (2001 Apr 5-11) 97 (14) 52.
Journal code: 0423236. ISSN: 0954-7762.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Nursing Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020417
Last Updated on STN: 20020508
Entered Medline: 20020507

L77 ANSWER 5 OF 36 MEDLINE
ACCESSION NUMBER: 96440059 MEDLINE
DOCUMENT NUMBER: 96440059 PubMed ID: 8842370
TITLE: Application of benzyl hyaluronate membranes as potential wound dressings: evaluation of water vapour and gas permeabilities.
AUTHOR: Ruiz-Cardona L; Sanzgiri Y D; Benedetti L M; Stella V J; Topp E M
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kansas, Lawrence 66045, USA.
SOURCE: BIOMATERIALS, (1996 Aug) 17 (16) 1639-43.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961230

AB Membranes of 75% and 100% benzyl hyaluronate esters (percentage of total carboxylate groups esterified) were prepared and their water vapour, oxygen and carbon dioxide transmission rates determined. The values of these properties were compared with the values obtained for several commercial wound dressings under the same conditions. The benzyl hyaluronate membranes showed water vapour transmission rates (2157-2327 gm-2 per day) comparable to those from commercial skin dressings (426-2047 gm-2 per day). In the dry state, the benzyl hyaluronate membranes showed lower oxygen and carbon dioxide transmission rates. Taking into account the biocompatibility of the hyaluronic acid esters, and the possibility that therapeutic agents could be incorporated into these membranes, the results indicate that the benzyl hyaluronate membranes have potential wound dressing applications.

L77 ANSWER 6 OF 36 MEDLINE
ACCESSION NUMBER: 92190407 MEDLINE
DOCUMENT NUMBER: 92190407 PubMed ID: 1799648
TITLE: In vitro studies on biocompatibility of hyaluronic acid esters.
AUTHOR: Cortivo R; Brun P; Rastrelli A; Abatangelo G
CORPORATE SOURCE: Institute of Histology, University of Padova, Italy.
SOURCE: BIOMATERIALS, (1991 Oct) 12 (8) 727-30.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 19920509
Last Updated on STN: 19920509
Entered Medline: 19920421

AB The biocompatibility of semisynthetic polymers formed from hyaluronic acid esters has been studied using fibroblast cultures. The polymers, added to the culture medium, used either in powdered form or as thin membranes, behave as inert materials. The cells used in the experiments grow normally in the culture dishes. With regard to adhesiveness the cells were not able to spread on the biomembranes and tended to form isolated clusters of round cells. Human fibronectin, placental collagen (type I-IV) and fibrin could be stratified on biomembranes. When these molecules reacted with the biomaterial the film became suitable for fibroblasts spreading and growth.

L77 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1994:227032 CAPLUS
DOCUMENT NUMBER: 120:227032
TITLE: Biodegradable guide channels for use in tissue repair as surgical aids
INVENTOR(S): Dorigatti, Franco; Favaro, Giorgio; Callegaro, Lanfranco; Romeo, Aurelio
PATENT ASSIGNEE(S): Fidia S.p.A., Italy
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403212	A1	19940217	WO 1993-EP2066	19930803
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 652778	A1	19950517	EP 1993-917733	19930803
EP 652778	B1	20000315		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07509386	T2	19951019	JP 1993-505011	19930803
AU 690891	B2	19980507	AU 1993-47064	19930803
AT 190507	E	20000415	AT 1993-917733	19930803
ES 2144460	T3	20000616	ES 1993-917733	19930803

PRIORITY APPLN. INFO.: IT 1992-PD144 A 19920803
WO 1993-EP2066 W 19930803

AB Medical devices are disclosed, comprising biodegradable guide channels for use in repair and regeneration of nerve tissue. The guide channels comprise interlaced threads embedded in a matrix optionally

contg. active factors, wherein both the matrix and the threads comprise biocompatible and bioabsorbable esters of hyaluronic acid.

IT **9004-61-9DP**, Hyaluronic acid, **esters 51434-20-9P**
, Methyl hyaluronate **111744-91-3P**, Pentyl hyaluronate
111744-92-4P, Benzyl hyaluronate **111744-93-5P**
111744-94-6P 111745-18-7P 111745-19-8P, Ethyl
hyaluronate **111745-26-7P 111745-27-8P**
111745-30-3P 111745-31-4P 111745-32-5P
150104-19-1P 150104-20-4P 150104-22-6P
150104-23-7P 150104-24-8P 150104-25-9P
150104-26-0P 150104-27-1P
RL: PREP (Preparation)
(prepn. of, as medical material for nerve **regeneration**)

L77 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:158403 CAPLUS
DOCUMENT NUMBER: 136:205509
TITLE: Hyaluronic acid esters, threads and **biomaterials** containing them, and their use in **surgery**
INVENTOR(S): Bellini, Davide; Callegaro, Lanfranco
PATENT ASSIGNEE(S): Italy
SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 236,958.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002026039	A1	20020228	US 2001-941055	20010828
US 2001008937	A1	20010719	US 1999-236958	19990125

PRIORITY APPLN. INFO.:
IT 1996-PD207 A 19960829
US 1999-236958 A2 19990125
WO 1997-EP4684 A1 19970828

AB The application discloses esters of hyaluronic acid, wherein a first part of the carboxylic functions is esterified with an araliph. alc. and a second part is esterified with at least one long-chain, straight C10-22 aliph. alc. The possible remaining non-esterified carboxylic functions, if present, are salified. The application further discloses biocompatible threads having a multifilament conformation comprising filaments formed by the hyaluronic acid esters in combination with other biocompatible polymers, such as PTFE, polyglycolic acid, polylactic acid, polycaprolactone, etc. The biocompatible threads are useful in medicine and surgery, as, e.g., sutures, scaffolds for cell culture in the form of gauzes, meshes, non-woven fabrics, tubes, etc. For example, a hyaluronic acid ester was prepd. by reacting 6.21 g of tetra-Bu ammonium salt of hyaluronic acid with 0.89 mL of benzyl bromide and 0.83 g of octadecyl bromide to obtain 5.1 g of hyaluronic acid benzyl octadecyl ester. A mixed multifilament was prepd. by extrusion of this ester in combination with a multifilament of PTFE.

IT **9004-61-9DP**, Hyaluronic acid, **esters**, salts
203798-22-5P 203874-06-0P, Hyaluronic acid benzyl
hexadecyl ester **203874-07-1P**, Hyaluronic acid benzyl octadecyl
ester **401810-52-4P**, Hyaluronic acid benzyl decyl ester
401810-53-5P, Hyaluronic acid benzyl eicosanyl ester sodium salt
401810-54-6P, Hyaluronic acid benzyl docosanyl ester sodium salt
RL: PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hyaluronic acid mixed **esters** and threads for **surgical biomaterials**)

L77 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:520184 CAPLUS
DOCUMENT NUMBER: 136:221679
TITLE: Transplantation of chondrocytes seeded on a hyaluronan derivative (Hyaff-11) into cartilage defects in rabbits
AUTHOR(S): Grigolo, B.; Roseti, L.; Fiorini, M.; Fini, M.; Giavaresi, G.; Nicoli Aldini, N.; Giardino, R.; Facchini, A.
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Istituto di Ricerca Codivilla-Putti, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), 22(17), 2417-2424
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Different methods have been used to improve chondrocyte transplantation for the repair of articular cartilage defects. Several groups of biomaterials have been proposed as support for in vitro cell growth and for in vivo implantation. Here, we describe a new approach investigating the healing of rabbit cartilage by means of autologous chondrocytes seeded on a hyaluronan deriv. referred to as Hyaff-11. Full thickness defects were created bilaterally in the wt.-bearing surface of the medial femoral condyle of both femora of New Zealand male rabbits. The wounds were then repaired using both chondrocytes seeded on the biomaterial and biomaterial alone. Controls were similarly treated but received either no treatment or implants of the delivery substance. Histol. samples from in and around the defect sites were examd. 1, 3 and 6 mo after surgery and were scored from 0 to 16. Statistically significant differences in the quality of the **regenerated** tissue were found between the grafts carried out with biomaterial carrying chondrocyte cells compared to the biomaterial alone or controls. This study demonstrates the efficacy of this hyaluronan-based scaffold for autologous chondrocytes transplantation.
IT **111744-92-4**, Hyaff-11
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transplantation of chondrocytes seeded on a hyaluronan deriv. (Hyaff-11) into cartilage defects in rabbits)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:861970 CAPLUS
DOCUMENT NUMBER: 137:145470
TITLE: Evidence for redifferentiation of human chondrocytes grown on a hyaluronan-based **biomaterial** (HYAFF11): molecular, immunohistochemical and ultrastructural analysis
AUTHOR(S): Grigolo, Brunella; Lisignoli, Gina; Piacentini, Anna; Fiorini, Mauro; Gobbi, Pietro; Mazzotti, Giovanni; Duca, Manuela; Pavesio, Alessandra; Facchini, Andrea
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Istituto di Ricerca Codivilla Putti, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), Volume Date 2002, 23(4), 1187-1195
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Assocn. of biomaterials with autologous cells can provide a new generation

of implantable devices for cartilage repair. Such scaffolds should provide a preformed **three-dimensional** shape and prevent cells from escaping into the articular cavity. Furthermore, these constructs should have sufficient mech. strength to facilitate handling in a clin. setting and stimulate the uniform spreading of cells and their phenotype redifferentiation. The aim of this study was to verify the ability of HYAFF11, a recently developed hyaluronic-acid-based biodegradable polymer, to support the growth of human chondrocytes and to maintain their original phenotype. This capability was assessed by the evaluation of collagen types I, II and aggrecan mRNA expression. Immunohistochem. analyses were also performed to evaluate collagen types I, II and proteoglycans synthesis. A field emission in lens scanning microscopy was utilized to verify the interactions between the cells and the biomaterial. The data indicate that human chondrocytes seeded on HYAFF11 express and produce collagen type II and aggrecan and downregulate the prodn. of collagen type I. These results provide an in vitro demonstration for the therapeutic potential of HYAFF11 as a delivery vehicle in a tissue-engineered approach towards the repair of articular cartilage defects.

IT **111744-92-4**, HYAFF11
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(redifferentiation of human chondrocytes grown on a hyaluronan-based **biomaterial** (HYAFF11))

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:861940 CAPLUS
DOCUMENT NUMBER: 137:145462
TITLE: Physico-chemical properties and degradability of non-woven hyaluronan benzylic esters as tissue engineering scaffolds
AUTHOR(S): Milella, E.; Brescia, E.; Massaro, C.; Ramires, P. A.; Miglietta, M. R.; Fiori, V.; Aversa, P.
CORPORATE SOURCE: Biomaterials Unit, PASTIS-CNRSM, Brindisi, Italy
SOURCE: Biomaterials (2001), Volume Date ~~2002, 23~~(4), 1053-1063
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The development of biocompatible materials which can be processed into **three-dimensional** scaffolds and the design of appropriate configurations in order to enable the cellular infiltration and proliferation is a major issue in the tissue engineering. The hyaluronan total benzyl ester (Hyaff11) has been found to be suitable substrate to ~~grow~~ a variety of cell types. Since structural, phys., chem. and biol. data can help for tailoring appropriate scaffold for tissue engineering, information on chemico-phys. properties on degradability of hyaluronan total benzyl ester non-woven has been obtained. The thermal anal., the evaluation of the surface chem. compn., the morphol., the mech. behavior and the swelling tests were carried out on these materials. The hyaluronan total benzyl ester non-woven showed a thermal stability up to 220.degree. and the surface compn. differed from that of the bulk for C-O and C-C contribution. No contaminant were detected. The non-woven swelled in culture medium. Moreover the mech. tests showed that when submitted to a press treatment, the samples have best mech. properties. The pressed Hyaff11 non-woven undergoes degrdn. when exposed to DMEM. The frying and breaking of the **fibers**, a decrease of the mech. properties and a mol. wt. loss have been obsd. First, the ester bond of the Hyaff11 non-woven is hydrolyzed and the benzylic alc. is released and the low mol. wt. values indicate that a cleavage of the polymer is

promoted by the components of the culture medium. After 11 days, some fragments, constituted by hyaluronic acid with a mol. wt. of 23,000 Da became sol. in the medium. No oligomer was detected.

IT **111744-92-4**, Hyaff11
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(physico-chem. properties and degradability of non-woven hyaluronan benzylic esters as tissue engineering scaffolds)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:662793 CAPLUS
DOCUMENT NUMBER: 136:374747
TITLE: Tissue-engineered fabrication of an osteochondral composite graft using rat bone marrow-derived mesenchymal stem cells
AUTHOR(S): Gao, Jizong; Dennis, James E.; Solchaga, Luis A.; Awadallah, Amad S.; Goldberg, Victor M.; Caplan, Arnold I.
CORPORATE SOURCE: Skeletal Research Center, Case Western Reserve University, Cleveland, OH, USA
SOURCE: Tissue Engineering (2001), 7(4), 363-371
CODEN: TIENFP; ISSN: 1076-3279
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study tested the tissue engineering hypothesis that construction of an osteochondral composite graft could be accomplished using multipotent progenitor cells and phenotype-specific biomaterials. Rat bone marrow-derived mesenchymal stem cells (MSCs) were culture-expanded and sep. stimulated with transforming growth factor-.beta.1 (TGF-.beta.1) for chondrogenic differentiation or with an osteogenic supplement (OS). MSCs exposed to TGF-.beta.1 were loaded into a sponge composed of a hyaluronan deriv. (HYAFF-11) for the construction of the cartilage component of the composite graft, and MSCs exposed to OS were loaded into a porous calcium phosphate ceramic component for bone formation. Cell-loaded HYAFF-11 sponge and ceramic were joined together with fibrin sealant, Tisseel, to form a composite osteochondral graft, which was then implanted into a s.c. pocket in syngeneic rats. Specimens were harvested at 3 and 6 wk after implantation, examd. with histol. for morphol. features, and stained immunohistochem. for type I, II, and X collagen. The two-component composite graft remained as an integrated unit after in **vivo** implantation and histol. processing. Fibrocartilage was obsd. in the sponge, and bone was detected in the ceramic component. Observations with polarized light indicated continuity of collagen **fibers** between the ceramic and HYAFF-11 components in the 6-wk specimens. Type I collagen was identified in the neo-tissue in both sponge and ceramic, and type II collagen in the fibrocartilage, esp. the pericellular matrix of cells in the sponge. These data suggest that the construction of a tissue-engineered composite osteochondral graft is possible with MSCs and different biomaterials and bioactive factors that support either chondrogenic or osteogenic differentiation.

IT **111744-92-4**, HYAFF-11
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sponge; tissue-engineered fabrication of an osteochondral composite graft using rat bone marrow-derived mesenchymal stem cells)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:449967 CAPLUS
DOCUMENT NUMBER: 134:9281

TITLE: Cartilage tissue engineering using scaffolds of hyaluronan benzyl esters for reconstructive head and neck **surgery**
AUTHOR(S): Aigner, Joachim; Staudenmaier, Rainer; Rotter, Nicole; Kloppel, Marcus; Radice, Marco; Pavesio, Alessandra; Naumann, Andreas
CORPORATE SOURCE: Department of Otorhinolaryngology, Ludwig-Maximilians-University of Munich, Munich, D-81377, Germany
SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 255-265
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tissue engineering techniques may offer the means to generate hyaline cartilage for reconstructive surgery and to repair articular defects. Our approach is based on the use of isolated auricular or nasoseptal chondrocytes, which are first expanded and then seeded on bioresorbable cell carriers allowing a **three-dimensional** (3-D) cell arrangement. While traditional cell culture techniques lead to the dedifferentiation of cells, cells cultured on 3-D scaffolds should reexpress their cartilage-specific phenotype. Since HA plays an essential role in cartilage matrix organization, our investigations focused on the redifferentiation capability of human and rabbit chondrocytes cultured on HYAFF-11, a nonwoven benzyl esterified hyaluronic acid deriv. Following xenogen implantation of human cells in nude mice, as well as autologous implantation of rabbit cells, chondrocytes regained their phenotype as demonstrated by re-expression of collagen type II. The data show that previously dedifferentiated chondrocytes regain their ability to express cartilage specific mols. when cultured in a 3-D structure on special cell carriers. Long-term studies should clarify the biol. effects of the cultured cells with respect to the degrdn. properties of the nonwoven scaffold. The biomaterial, HYAFF-11, available in versatile forms and structures, provides promising opportunities for the prodn. of custom-designed scaffolds in tissue engineering procedures.
IT **111744-92-4**, HYAFF-11
RL: DEV (Device component use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cartilage tissue engineering using scaffolds of hyaluronan benzyl esters for reconstructive head and neck **surgery**)
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:449966 CAPLUS
DOCUMENT NUMBER: 134:9280
TITLE: Chondrogenic differentiation of mesenchymal stem cells on matrixes of hyaluronan derivatives
AUTHOR(S): Barry, Frank P.; Murphy, J. Mary
CORPORATE SOURCE: Osiris Therapeutics Inc., Baltimore, MD, 21231, USA
SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 247-253
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mesenchymal stem cells derived from bone marrow have the capacity to differentiate into chondrocytes when cultured under appropriate conditions and offer significant opportunities for **regeneration** of cartilage lesions in joint disease. Hyaluronan derivs. may be used as

construct materials to support the growth and differentiation of stem cells and allow them to be delivered to the site of injury. HYAFF-11 was evaluated as a potential vehicle for such a delivery by detg. the ability of the material, both in a sponge and fabric format, to support differentiation of stem cells. When cultured on these materials without serum and with added TGF-.beta.3 stem cells were capable of differentiating into chondrocytes with rapid deposition of a proteoglycan- and collagen II-rich extracellular matrix.

IT **111744-92-4**, HYAFF-11
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chondrogenic differentiation of mesenchymal stem cells on matrixes of hyaluronan derivs.)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:449965 CAPLUS
DOCUMENT NUMBER: 134:61422
TITLE: Hyaluronic acid-based **biomaterials** in tissue engineered cartilage repair
AUTHOR(S): Solchaga, Luis A.; Goldberg, Victor M.; Caplan, Arnold I.
CORPORATE SOURCE: Skeletal Research Center, Case Western Reserve University School of Medicine, Cleveland, OH, 44106-7080, USA
SOURCE: International Congress Series (2000), 1196(New Frontiers in Medical Sciences: Redefining Hyaluronan), 233-246
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Articular cartilage in adults has limited ability for self-repair. Some methods devised to augment the natural healing response stimulate some **regeneration**, but the repair is often incomplete and lacks durability. Hyaluronic acid (HA)-based polymers were tested for their ability to enhance the natural healing response. Our hypothesis is that HA-based polymers recreate an embryonic-like milieu, in which host progenitor cells can **regenerate** the damaged articular surface and underlying bone. Osteochondral defects were made on the femoral condyles of 4-mo-old rabbits and were left empty or filled with HA-based polymers that were loaded or not with either autologous bone marrow (BM) or autologous mesenchymal progenitor cells (MPCs). The polymers tested were ACP and HYAFF-11 (provided by Fidia Advanced Biopolymers; Abano Terme, Italy). Rabbits were sacrificed at various time points after surgery and the condyles processed for histol. Untreated defects filled with bony tissue up to or beyond the tidemark, and the noncalcified surface layer varied from fibrous to hyaline-like tissue. Four weeks after surgery, defects treated with ACP exhibited bony filling to the level of the tidemark, and the surface layer was composed of hyaline-like cartilage that was well-integrated with the adjacent cartilage. The 12-wk specimens presented bone beyond the tidemark that was covered with a thin layer of hyaline cartilage. Four weeks after surgery, defects treated with HYAFF-11 contained a rim of chondrogenic cells at the interface with host tissue. In general, by 12 wk the defects exhibited good bony fill, and the surface was mainly hyaline cartilage. We conclude that the introduction of these HA-based polymers into defects provides an appropriate scaffolding and favorable microenvironment for the reparative process. Further work is required to fully assess the long-term outcome of defects treated with these polymers.

IT **111744-92-4**, HYAFF-11
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hyaluronic acid-based **biomaterials** in tissue engineered

cartilage repair)
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:161838 CAPLUS
DOCUMENT NUMBER: 132:313587
TITLE: Hyaluronan-based biopolymers as delivery vehicles for bone-marrow-derived mesenchymal progenitors
AUTHOR(S): Radice, M.; Brun, P.; Cortivo, R.; Scapinelli, R.; Battaliard, C.; Abatangelo, G.
CORPORATE SOURCE: Institute of Histology and Embryology, University of Padova, Padua, I-35121, Italy
SOURCE: Journal of Biomedical Materials Research (2000), 50(2), 101-109
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tolerability and safety of hyaluronan-based **3-dimensional** scaffolds as a culture vehicle for mesenchymal progenitor cells was investigated in this pilot study. The proliferation patterns and extracellular matrix prodn. of rabbit and human mesenchymal, bone-marrow-derived progenitors first were characterized in vitro. Subsequently rabbit autologous cells were cultured in this hyaluronan-based scaffold and implanted in a full-thickness osteochondral lesion. In vitro histol. findings showed that mesenchymal progenitor cells adhered and proliferated onto the hyaluronan-derived scaffold. Human stem cells produced the main extracellular matrix mols., accompanied by an occasional synthesis of mature type II collagen. In **vivo** data demonstrated that the biomaterial, with or without mesenchymal progenitors, did not elicit any inflammatory response and was completely degraded within 4 mo after implantation. With regard to the efficacy of this cell therapy, even among the small no. of animals tested there was histol. evidence that lesions filled with the biomaterial, either seeded or unseeded with cells, achieved a faster and better healing compared to empty controls. The present data suggest that the hyaluronan-based scaffolds are well tolerated and safe and may be a valuable delivery vehicle for tissue engineering in the repair of articular cartilage defects.
IT **111744-92-4**, Hyaff 11
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hyaluronan-based biopolymers as delivery vehicles for bone-marrow-derived mesenchymal progenitors)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:414463 CAPLUS
DOCUMENT NUMBER: 131:174989
TITLE: Chondrocyte aggregation and reorganization into three-dimensional scaffolds
AUTHOR(S): Brun, Paola; Abatangelo, Giovanni; Radice, Marco; Zacchi, Valentina; Guidolin, Diego; Gordini, Daniela Daga; Cortivo, Roberta
CORPORATE SOURCE: Institute of Histology and Embryology, Faculty of Medicine, University of Padova, Padua, I-35121, Italy
SOURCE: Journal of Biomedical Materials Research (1999), 46(3), 337-346
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: English

AB Articular cartilage has a very limited self-repairing capacity; thus, chondral lesions normally result in chronic degeneration and, eventually, osteoarthritis development. Currently, tissue engineering offers a new tool for the clin. treatment of osteochondral defects. The present investigation aimed to develop an in vitro engineered cartilage using a new class of semisynthetic scaffolds. Two non-woven meshes of hyaluronan esters (Hyaff derivs.) were seeded with sternal chick embryo chondrocytes cultured for up to 21 days, after which time they were assessed for both the cellular growth profile and histol. features. Avian chondrocytes easily adhered and proliferated onto hyaluronan-based scaffolds, demonstrating a significant preference for the fully esterified benzylic form. Histochem. staining revealed the presence of a neo-synthesized glycosaminoglycan-rich extracellular matrix, and immunohistochem. confirmed the deposition of collagen type II. Moreover, ultrastructural observations supported evidence that chondrocytes grown onto a hyaluronan-derived three-dimensional scaffold maintained their unique phenotype and organization in a cartilage-like extracellular matrix. These findings support the further pursuit of a transplantable engineered cartilage using human chondrocytes for the **regeneration** of chondral lesions.

IT **111744-92-4**, Hyaff 11 **111745-19-8**, Hyaff 7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(non-woven meshes; chondrocyte aggregation and reorganization into 3-dimensional scaffolds)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:163621 CAPLUS
DOCUMENT NUMBER: 128:206127
TITLE: Hyaluronic acid esters, threads and **biomaterials** containing them, and their use in **surgery**
INVENTOR(S): Callegaro, Lanfranco; Bellini, Davide
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Italy; Callegaro, Lanfranco; Bellini, Davide
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808876	A1	19980305	WO 1997-EP4684	19970828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9742080	A1	19980319	AU 1997-42080	19970828
AU 722586	B2	20000810		
EP 922060	A1	19990616	EP 1997-940137	19970828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
JP 2000516978	T2	20001219	JP 1998-511290	19970828
US 2001008937	A1	20010719	US 1999-236958	19990125

PRIORITY APPLN. INFO.: IT 1996-PD207 A 19960829

WO 1997-EP4684 W 19970828

AB The hyaluronic acid esters have a first part of the carboxy functions esterified with an aliph. alc. and a second part esterified with long-chain, straight aliph. alcs. with 10-22 C atoms. The possible remaining non-esterified carboxy functions, if present, are salified. The esters are processed into biodegradable threads which are useful for the fields of medicine and surgery. Thus, benzylating a hyaluronic acid tetrabutylammonium salt (mol. wt. 189,000 Dalton) dissolved in DMSO with PhCH2Br then alkylating with dodecyl bromide gave a hyaluronic acid mixed ester which was spun from a DMSO soln. to give multifilament threads.

IT **203798-22-5P**, Hyaluronic acid benzyl lauryl ester
203874-06-0P, Hyaluronic acid benzyl palmityl ester
203874-07-1P, Hyaluronic acid benzyl stearyl ester
203874-08-2P, Hyaluronic acid benzyl arachidyl ester
203874-09-3P, Hyaluronic acid benzyl docosanyl ester
RL: IMF (Industrial manufacture); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(manuf. and use in threads and **biomaterials**)

L77 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:265578 CAPLUS
DOCUMENT NUMBER: 126:255537
TITLE: **Biomaterials** for preventing post-**surgical** ~~adhesions comprised~~ of hyaluronic acid derivatives
INVENTOR(S): Pressato, Daniele; Pavesio, Alessandra; Callegaro, Lanfranco
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers, S.R.L., Italy; Pressato, Daniele; Pavesio, Alessandra; Callegaro, Lanfranco
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9707833	A2	19970306	WO 1996-EP3805	19960829
WO 9707833	A3	19970410		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2230530	AA	19970306	CA 1996-2230530	19960829
AU 9669300	A1	19970319	AU 1996-69300	19960829
AU 718484	B2	20000413		
EP 850074	A2	19980701	EP 1996-930132	19960829
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1199343	A	19981118	CN 1996-197522	19960829
BR 9610996	A	19990713	BR 1996-10996	19960829
JP 11511344	T2	19991005	JP 1996-509858	19960829
RU 2177332	C2	20011227	RU 1998-105612	19960829
NO 9800888	A	19980427	NO 1998-888	19980227

PRIORITY APPLN. INFO.: IT 1995-PD166 A 19950829
IT 1995-PD167 A 19950829
WO 1996-EP3805 W 19960829

AB New biomaterials essentially constituted by esterified derivs. of hyaluronic acid or by crosslinked derivs. of hyaluronic acid for use in

the surgical sector, particularly for use in the prevention of post-surgical adhesions, are provided. A soln. of hyaluronic acid benzyl ester in DMSO at 135 mg/mL was prepd. and fed into a spinneret for wet extrusion and the extruded mass of threads was passed into a coagulation bath contg. abs. ethanol. The hank of threads was blown dry and cut into 40 mm **fibers**, which were made into a web. The web was then sprayed with a soln. of hyaluronic acid benzyl ester in DMSO at 80 mg/mL, placed in an ethanol coagulation bath, in a rinsing chamber, and lastly in a drying chamber, to give a nonwoven fabric with a thickness of 0 5 mm.

IT **9004-61-9DP**, Hyaluronic acid, mixed **esters**
111744-92-4P, Hyaluronic acid benzyl ester **111745-19-8P**,
Hyaluronic acid ethyl ester
RL: PNU (Preparation, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(**biomaterials** for preventing post-**surgical** adhesions comprised of hyaluronic acid derivs.)

L77 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:638467 CAPLUS
DOCUMENT NUMBER: 121:238467
TITLE: Multilayer nonwoven tissue containing a surface layer comprising at least one hyaluronic acid ester
INVENTOR(S): Dorigatti, Franco; Callegaro, Lanfranco
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.L., Italy
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9417837	A1	19940818	WO 1994-EP397	19940211
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2155319	AA	19940818	CA 1994-2155319	19940211
AU 9461088	A1	19940829	AU 1994-61088	19940211
AU 681873	B2	19970911		
EP 683679	A1	19951129	EP 1994-907550	19940211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08506255	T2	19960709	JP 1994-517674	19940211
IL 110438	A1	19980924	IL 1994-110438	19940725
CN 1116085	A	19960207	CN 1994-116145	19940730
US 5658582	A	19970819	US 1995-505325	19951010

PRIORITY APPLN. INFO.: IT 1993-PD24 19930212
WO 1994-EP397 19940211

AB A multilayer nonwoven material, comprising a surface layer which comes into contact with the skin, such as hyaluronic acid ester, and one or more other layers which do not come into contact with the skin. This material can be employed in a wide variety of medical and sanitary applications, including surgery and as a non-adhesive covering material. A multilayer nonwoven tissue composed of a layer of hyaluronic acid benzyl ester (Hyaff 11) and a layer of nonwoven viscose (Jettex 2005), with 2mm thickness and water absorption of 56% was prepd.

IT **9004-61-9D**, Hyaluronic acid, **esters 111744-92-4**
, Hyaluronic acid benzyl ester **111745-19-8**, Hyaluronic acid ethyl ester
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(multilayer nonwoven tissue contg.)

L77 ANSWER 21 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001224947 EMBASE
TITLE: Recessive epidermolysis bullosa dystrophicans (Hallopeau-Siemens) - Improvement of wound healing by autologous epidermal grafts on an esterified hyaluronic acid membrane.
AUTHOR: Wollina U.; Konrad H.; Fischer T.
CORPORATE SOURCE: U. Wollina, Department of Dermatology, Medical School, Friedrich-Schiller-Univ. of Jena, Erfurter Strasse 35, 07740 Jena, Germany
SOURCE: Journal of Dermatology, (2001) 28/4 (217-220).
Refs: 15
ISSN: 0385-2407 CODEN: JDMYAG
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
013 Dermatology and Venereology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Epidermolysis bullosa dystropicans of the Hallopeau-Siemens type (HS-EBD) is an autosomal-recessive blistering disease. Skin fragility due to mutations in structural proteins is responsible for further development of chronic and painful wounds, skin infections and sepsis. There is no causative treatment available. We present a case report with HS-EBD and longstanding painful wounds treated with autologous keratinocytes on an esterified hyaluronic acid membrane. Two out of three wounds treated showed a complete take of the graft. They improved markedly with a stable result over 12 months until now. Even autologous keratinocyte grafting may have a beneficial effect on chronic wounds in HS-EBD despite the fact that the genetic defects are unchanged.

L77 ANSWER 22 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000409431 EMBASE
TITLE: Biocompatibility and biodegradation of intravitreal hyaluronan implants in rabbits.
AUTHOR: Avitabile T.; Marano F.; Castiglione F.; Bucolo C.; Cro M.; Ambrosio L.; Ferrauto C.; Reibaldi A.
CORPORATE SOURCE: C. Bucolo, Fidia Oftal, Research Laboratories, Corso Italia 141, 95127 Catania, Italy. bucocla@mbox.unict.it
SOURCE: Biomaterials, (2001) 22/3 (195-200).
Refs: 20
ISSN: 0142-9612 CODEN: BIMADU
PUBLISHER IDENT.: S 0142-9612(00)00169-1
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
039 Pharmacy
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To study the biocompatibility and the biodegradation rate in vivo of new intravitreal implants made with three different hyaluronic acid esters: Hyaff7, Hyaff11 and Hyaff11p75 (100% ethyl ester, 100 and 75% benzyl esters, respectively), the plugs were implanted through a sclerotomy at 3.5mm from the limbus of rabbit eyes. In order to evaluate the in vivo biodegradation the shaft diameter of the plugs was measured by ultrasound biomicroscopy. Slit lamp microscopy, ophthalmoscopy and ERG were performed periodically. The effects of the implants on ocular tissues were also evaluated histologically. All the plugs showed a good biocompatibility.

Plugs of both the total esters, Hyaff7 and Hyaff11, were found to undergo a slow dissolution process for 60 and 150 days, respectively. The partial benzyl ester, Hyaff11p75, was completely reabsorbed after 15 days. Analysis of variance showed a high correlation between biodegradation rate and the time of resorption ($F=90.5$; $p<0.001$). The biodegradation rate of each implant is related to the chemical structure of the three types of Hyaff ($F=4.51$; $p=0.005$). The present data suggest that intravitreal implants based on hyaluronic acid esters represent useful biocompatible and biodegradable devices for a potential drug delivery system in the treatment of posterior segment ocular diseases. Copyright (C) 2000 Elsevier Science B.V.

L77 ANSWER 23 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999414118 EMBASE
TITLE: In vitro reconstructed tissues on hyaluronan-based temporary scaffolding.
AUTHOR: Brun P.; Cortivo R.; Zavan B.; Vecchiato N.; Abatangelo G.
CORPORATE SOURCE: G. Abatangelo, Institute Histology and Embryology, Faculty of Medicine, University of Padova, Viale G. Colombo 3, 35121 I-Padova, Italy. abatange@civ.bio.unipd.it
SOURCE: Journal of Materials Science: Materials in Medicine, (1999) 10/10-11 (683-688).
Refs: 62
ISSN: 0957-4530 CODEN: JSMMEL
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
013 Dermatology and Venereology
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tissue engineering offers the possibility to reconstruct tissue substitutes in order to replace lost or damaged tissues. The availability of appropriate biomaterial devices is essential to allow in vitro cultured cells to behave as in the original tissues in vivo. In our studies we utilized a seminatural biomaterial made up by the benzyl ester of hyaluronan to grow keratinocytes, fibroblasts and chondrocytes. Keratinocytes and fibroblasts were isolated from human foreskin. Cells were separately cultured on two different hyaluronan based biomaterial devices for the first 15 days and then co-cultured for an additional period of 2 weeks. Keratinocytes gave rise to a well-differentiated epithelial layer, while fibroblasts were able to synthesize all the main extracellular molecules inside the biomaterial spaces, forming dermal-like tissues. When these two tissues were co-cultured, a skin equivalent was formed with a dermal-epidermal junction. Chondrocytes were obtained from chick-embryo sterna and cultured for 21 days inside a non-woven scaffolding made up of a hyaluronan-based biomaterial. Cells were able to organize themselves into nodules embedded in a dense metachromatic substance in which type II collagen was present. Data from this study suggest that this novel class of hyaluronan derived biomaterials is suitable for different cell culture and in vitro tissue reconstruction.

L77 ANSWER 24 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96160646 EMBASE
DOCUMENT NUMBER: 1996160646
TITLE: Quantitative assessment of the tissue response to films of hyaluronan derivatives.
AUTHOR: Campoccia D.; Hunt J.A.; Doherty P.J.; Zhong S.P.; O'Regan M.; Benedetti L.; Williams D.F.
CORPORATE SOURCE: Department of Clinical Engineering, University of Liverpool, PO Box 147,Liverpool L69 3BX, United Kingdom
SOURCE: Biomaterials, (1996) 17/10 (963-975).

ISSN: 0142-9612 CODEN: BIMADU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The aim of this study was to evaluate the in vivo response following implantation into a rat model of three innovative hyaluronan derivatives for clinical use: HYAFF 7, HYAFF 11 and HYAFF 11p75 (respectively, the 100% ethyl ester, 100% and 75% benzyl esters). The tissue reaction evoked by films of these new biomaterials implanted into the dorsolumbar musculature of rats was assessed quantitatively using a well established technique based upon an image analysis system. The number of inflammatory cells present and the patterns of cell distribution around the implant up to a distance of 642 .mu.m were examined at different time periods after implantation. Since a well-delineated tissue-material interface was needed for this type of investigation, it was not possible to apply image analysis to sections once dissolution of the implanted materials had begun. Films of both the total esters, HYAFF 7 and HYAFF 11, were found to undergo a slow dissolution process and, after a month, films of these materials were still present at the site of implantation. Differences in response to the two materials were observed only during the first two weeks, particularly with respect to neutrophil distribution and total cellularity. HYAFF 7 was found to be more reactive, with higher numbers of neutrophils near the surface of the implant than HYAFF 11. Thereafter, the differences between the two materials were minimal and owing mainly to a faster dissolution of HYAFF 7 films. After 3 and 5 months, considerable degradation of films of both total esters had occurred. Significant quantities of material appeared inside numerous macrophages with an ED1-positive phenotype. Only a very thin layer of fibrous connective tissue, indicative of low reactivity, was found to surround the site of implantation, separating the dissolved material and the phagocytic cells from healthy muscular tissue. ED2-positive macrophages were primarily confined within the lining connective tissue. The partial benzyl ester, HYAFF 11p75, showed a different behaviour. In fact, evidence of film dissolution was already present a week after the implantation. After two weeks, the implanted films were completely dissolved and numerous ED1-positive macrophages phagocytosing the material were observed at the site of implantation. Therefore, in agreement with previous in vitro studies, which showed a greater susceptibility to degradation of hyaluronan derivatives with lower percentage of esterification, HYAFF 11p75 underwent resorption faster than the corresponding total ester.

L77 ANSWER 25 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94072096 EMBASE
DOCUMENT NUMBER: 1994072096
TITLE: Biocompatibility and biodegradation of different hyaluronan derivatives (Hyaff) implanted in rats.
AUTHOR: Benedetti L.; Cortivo R.; Berti T.; Berti A.; Pea F.; Mazzo M.; Moras M.; Abatangelo G.
CORPORATE SOURCE: Inst of Histology and Embryology, University of Padova, 75 via Trieste,Padova, Italy
SOURCE: Biomaterials, (1993) 14/15 (1154-1160).
ISSN: 0142-9612 CODEN: BIMADU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hyaluronan (HL), a naturally occurring glycosaminoglycan, has been chemically modified through the esterification of its carboxylic groups

with different types of alcohol. The physico-chemical properties of these new biopolymers allow the preparation of many biomaterials which may be used in several medical applications. In the present study both the biocompatibility and blodegradation of some water-insoluble HL esters have been evaluated, either as raw material or as manufactured devices after subcutaneous and intraperitoneal implantation in male rats. The inflammatory response and the degree of resorption for each tested material are reported. The relationships between the degree of esterification and the type of alcohol used with the above parameters are also investigated.

L77 ANSWER 26 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-329761 [36] WPIDS
DOC. NO. NON-CPI: N2002-258810
DOC. NO. CPI: C2002-095325
TITLE: New cross-linked derivative of partially N-deacetylated hyaluronic acid or its derivative useful in the preparation of e.g. biomaterial, pharmaceutical preparation.
DERWENT CLASS: A11 A96 B04 B07 D16 D22 P34
INVENTOR(S): CRESCENZI, V; FRANCESCANGELI, A; RENIER, D
PATENT ASSIGNEE(S): (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002018450	A1	20020307	(200236)*	EN	28
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002013870	A	20020313	(200249)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002018450	A1	WO 2001-EP10063	20010831
AU 2002013870	A	AU 2002-13870	20010831

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002013870	A Based on	WO 200218450

PRIORITY APPLN. INFO: IT 2000-PD207 20000831
AB WO 200218450 A UPAB: 20020610
NOVELTY - New cross-linked derivative (a) of partially N-deacetylated hyaluronic acid or its derivative comprises at least one repeating unit.
DETAILED DESCRIPTION - New cross-linked derivative of partially N-deacetylated hyaluronic acid or its derivative comprises at least one repeating unit of formula (I).
R1 = H or optionally substituted 1-20C residue derived from an aldehyde of G;
R2 = optionally substituted G;
R = OH, O- or an alcoholic, or amino group of G;
G = aromatic, (aryl)aliphatic, cycloaliphatic or heterocyclic series;
R3 = H, SO3-, a residue or heavy metal salts of hemiesters of

succinic acid;
R4 = COR or CH2OR3.
With the proviso that for R1 the aldehyde is liquid at room temperature.
INDEPENDENT CLAIMS are also included for the following:
(1) preparation of (a);
(2) a biomaterial comprising at least one (a) optionally in association with a natural, a (semi)synthetic polymer, or biologically or pharmacologically active substance (A);
(3) use of the biomaterial in association with (A) as vehicling agent for the preparation of slow release pharmaceutical compositions;
(4) a pharmaceutical composition comprising (a) as the active agent optionally in association with (A) and excipient and/or diluent; and
(5) use of (a) in association with radioactive and non-radioactive substances to be used in contrast systems, for the preparation of markers in vivo diagnostics for the identification and treatment of tumoral or damaged tissues.
USE - In the preparation of a biomaterial, which is useful as a healthcare or surgical article selected from microspheres, nanospheres, membranes, sponges, threads, films, gauzes, guide channel, hydrogel, non-woven tissue, felt, and their associations; a scaffold for cell cultures; for use in surgery (e.g. pelvic, abdominal, spinal, cardiac, vascular, ophthalmic, orthopaedic, otorhinolaryngological and plastic-aesthetic surgery), haemodialysis, cardiology, angiology, dermatology, ophthalmology, otorhinolaryngology, dentistry, orthopaedics, gynaecology, urology, in extracorporeal blood circulation and oxygenation, and in cosmetics; as a filler in plastic-aesthetic surgery; as substitutes for the vitreous humor in ophthalmology; useful in the prevention of surgical adhesions of tissues and hypertrophic scars; for the preparation of surgical glues; and as vehicling agent for the preparation of slow release pharmaceutical composition); for coating a biomedical object (e.g. bypass, venous catheter, shunt, catheter, guide channel, probe, cardiac valve, artificial tendon, bone and cardiovascular replacements, contact lens, soft tissue replacement, replacements of animal origin, blood oxygenators, artificial kidney, heart, pancreas and liver, blood bag, syringe, surgical instrument, filtration system, laboratory instrument, containers for cells and tissues cultures and for the **regeneration** of cells and tissues, support for peptides, proteins and antibodies and in healthcare and surgical articles (e.g. microspheres, nanospheres, membranes, sponges, threads, films, gauzes, guide channels, hydrogels, non-woven tissues, felts, and their associations); in a pharmaceutical preparation and in association with radioactive and non-radioactive substances to be used in contrast systems, for the preparation of markers in vivo diagnostics for the identification and treatment of tumoral or damaged tissues (claimed).
ADVANTAGE - (a) exhibits different chemical-physical properties according to the degree to which they are crosslinked.
Dwg.0/0

L77 ANSWER 27 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-308764 [35] WPIDS
CROSS REFERENCE: 2001-640226 [74]
DOC. NO. NON-CPI: N2002-241658
DOC. NO. CPI: C2002-089886
TITLE: Water swellable polymer gel for use in medical material, is formed by reacting esterified carboxy group containing polysaccharide with natural amino acid containing compound having two alpha-amino groups.
DERWENT CLASS: A11 A96 D22 P34
PATENT ASSIGNEE(S): (KURS) KURARAY CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2001278984 A		20011010	(200235)*		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2001278984 A		JP 2001-12081	20010119

PRIORITY APPLN. INFO: JP 2000-15381 20000125; JP 2000-14626 20000124

AB JP2001278984 A UPAB: 20020603
NOVELTY - A water swellable polymer gel is formed by reacting esterified carboxy group containing polysaccharide with a natural amino acid containing compound having at least two alpha -amino groups
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (i) A medical material comprising the water swellable polymer gel; (ii) Water swellable polymer gel foam formed by foaming water swellable polymer gel; and (ii) A method for manufacturing water swellable polymer gel, which involves esterifying carboxy group containing polysaccharide with natural amino acid containing compound having at least two alpha amino groups.
USE - For use in medical material, such as surgical dressing, adhesion prevention material, as tissue **regeneration** material (all claimed), haemostatic material, binding material, sealant, microcapsule material etc. Also used in food industries and agriculture.
ADVANTAGE - Since the polymer gel is manufactured by using natural derived components, the gel is highly safe for human body. The gel has excellent physical properties, such as high water absorbing capacity, mechanical strength, degree of swelling and favorable viscosity. The polymer gel is manufactured in high yield efficiently and economically.
Dwg.0/0

L77 ANSWER 28 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-640226 [74] WPIDS
CROSS REFERENCE: 2002-308764 [05]
DOC. NO. NON-CPI: N2001-478667
DOC. NO. CPI: C2001-189507
TITLE: Water-swellable polymer gel used in wound dressing, is obtained by reacting ester of carboxyl group containing polysaccharide with compound having two alpha-amino groups, derived from natural amino acid.
DERWENT CLASS: A11 A23 A96 A97 B07 C07 D22 P34
INVENTOR(S): FUJITA, A
PATENT ASSIGNEE(S): (KURS) KURARAY CO LTD
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1120428	A2	20010801	(200174)*	EN	14
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2001018464	A1	20010830	(200174)		
KR 2001076418	A	20010811	(200212)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1120428	A2	EP 2001-101182	20010124

US 2001018464 A1 US 2001-767227 20010123
KR 2001076418 A KR 2001-3389 20010120

PRIORITY APPLN. INFO: JP 2000-14626 20000124
AB EP 1120428 A UPAB: 20020603
NOVELTY - A water-swellable polymer gel is obtained by reacting an ester of a carboxyl group containing polysaccharide with a compound having at least two alpha -amino groups, derived from a natural amino acid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a material for medical use made of the water-swellable polymer gel;

(2) a foam containing water-swellable polymer gel prepared by foaming the gel; and

(3) a process for preparing a water-swellable polymer gel, which involves reacting an ester of carboxyl group containing polysaccharide with a compound having at least two alpha -amino groups, derived from a natural amino acid.

ACTIVITY - Vulnerary.

Japanese white rabbit (about 3.5 kg) was provided with apellous wound (of diameter 6 mm) on both ears. The obtained foam was applied on wounds and the entire surface of wound was covered with a polyurethane film and the film was fixed by suture. A comparative sample was prepared by covering wounds by foam prepared by using calcium alginate gel. The rabbits were fed with water and food at constant temperature. Subsequently the rabbits were sacrificed after 7 days and the wounds were collected. The tissues of the wounds were fixed, stained and observed under microscope. The results showed that the epithelial gap of wound covered by the flexible foam was found to be 1.8 mm and the calcium alginate gel covered wound was found to have epithelial gap of

MECHANISM OF ACTION - None given.

USE - As material for medical use, such as wound dressing, adhesion-preventing material or material for tissue **regeneration** (claimed) (e.g. as an extracellular matrix for **regeneration** of skin, mucosa, bones, cartilage, blood vessels, valves, nerves or cornea), dialysis membrane, hemostatic material, adhesive material, sealant, for making contact lenses, microcapsule material and drug delivery systems. Medicinally the gel is incorporated with physiologically active substance, such as heparin, dermatan sulfate, heparan sulfate, cytokine, anti-inflammatory agent, growth factor, enzyme, anti-bacterial agent or a living cell for administering to human. Also used in fields such as industries, agriculture, food and medicine.

ADVANTAGE - The polymeric gel is highly safe and is effectively decomposed in human body. The polymeric gel is water insoluble and has excellent water adsorbability, transparency, gel strength, mechanical property and high productivity. The water swellable polymeric gel is inexpensive and can is prepared effectively.

Dwg.0/0

L77 ANSWER 29 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-442544 [38] WPIDS
DOC. NO. NON-CPI: N2000-330171
DOC. NO. CPI: C2000-134665
TITLE: Injectable biocompatible compositions, used for cartilage repair and gene therapy, comprise hyaluronic acid derivative(s) and biologically or pharmacologically active components and/or mammalian cells.
DERWENT CLASS: B02 B04 D16 D22 P34
INVENTOR(S): CALLEGARO, L; PASTORELLO, A; PAVESIO, A; RADICE, M
PATENT ASSIGNEE(S): (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL; (CALL-I) CALLEGARO L; (PAST-I) PASTORELLO A; (PAVE-I) PAVESIO A; (RADI-I) RADICE M

COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000037124	A1	20000629	(200038)*	EN	43
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000017916	A	20000712	(200048)		
EP 1140240	A1	20011010	(200167)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
IT 1302534	B	20000905	(200215)		
US 2002076810	A1	20020620	(200244)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000037124	A1		WO 1999-IB2077	19991221
AU 2000017916	A		AU 2000-17916	19991221
EP 1140240	A1		EP 1999-961237	19991221
			WO 1999-IB2077	19991221
IT 1302534	B		IT 1998-PD298	19981221
US 2002076810	A1	Cont of	WO 1999-IB2077	19991221
			US 2001-887757	20010621

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000017916	A	Based on	WO 200037124
EP 1140240	A1	Based on	WO 200037124

PRIORITY APPLN. INFO: IT 1998-PD298 19981221

AB WO 200037124 A UPAB: 20000811
NOVELTY - Injectable biocompatible compositions comprising at least one hyaluronic acid derivative and at least one biologically or pharmacologically active component and/or mammalian cell.

DETAILED DESCRIPTION - Injectable biocompatible compositions comprise at least one hyaluronic acid derivative and at least one biologically or pharmacologically active component and/or mammalian cell. The hyaluronic acid derivative is a benzyl **ester** of **hyaluronic acid** in which 50-75% of the carboxy groups are esterified with a benzyl radical or an auto-crosslinked derivative of hyaluronic acid in which 3-15% of the carboxyl groups of hyaluronic acid are crosslinked to the hydroxyl group of the same or different hyaluronic acid molecule.

ACTIVITY - Vulnerary; uropathic; immunosuppressive; antidiabetic; antiarthritic; antirheumatic. Assays are described, but no results given.

MECHANISM OF ACTION - None given.

USE - The compositions are used for repair of cartilages (claimed) such as joint cartilages. They can be used to treat both superficial and deep cartilage defects. They may also be used to deliver cells for a variety of purposes e.g. fibroblasts (autologous) for aesthetic surgical purposes and as fillers for tissue defects, adipocytes (autologous, heterologous or homologous) for soft-tissue augmentation for applications such as reconstruction of breasts or other soft body parts, urethral cells (fibroblastoids or cartilage cells) to treat urinary incontinence and to treat autoimmune diseases such as juvenile diabetes or rheumatoid

arthritis. They may also be used for gene therapy to treat e.g. cystic fibrosis.

ADVANTAGE - The compositions are injectable, biocompatible and biodegradable. The hyaluronic acid-based material provides both a vehicle for injection and a method of protecting the cells during transport. The cell survival rate is higher than in prior art compositions improving transportability. The compositions can be spread more efficiently over the surface to be treated, allowing the **regenerated** tissue to integrate perfectly with the cartilage tissue surrounding the defect. The compositions do not need to be used immediately after preparation.
Dwg.0/0

L77 ANSWER 30 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-303127 [26] WPIDS
CROSS REFERENCE: 2000-292769 [24]
DOC. NO. NON-CPI: N2000-226533
DOC. NO. CPI: C2000-091848
TITLE: New hydrogel compositions useful for drug delivery or as temporary tissues scaffolds, comprises cross-linked hyaluronic acid derivatives.
DERWENT CLASS: A11 A96 B04 B07 D16 D22 P34
INVENTOR(S): AESCHLIMANN, D; BULLPITT, P; BULPITT, P
PATENT ASSIGNEE(S): (AESC-I) AESCHLIMANN D; (BULP-I) BULPITT P; (ORTH-N) ORTHOGENE LLC
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000016818	A1	20000330	(200026)*	EN	63
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 9961922	A	20000410	(200035)		
EP 1115433	A1	20010718	(200142)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000016818	A1	WO 1999-EP6913	19990917
AU 9961922	A	AU 1999-61922	19990917
EP 1115433	A1	EP 1999-948783	19990917
		WO 1999-EP6913	19990917

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9961922	A	Based on	WO 200016818
EP 1115433	A1	Based on	WO 200016818

PRIORITY APPLN. INFO: US 1998-156829 19980918
AB WO 200016818 A UPAB: 20000531
NOVELTY - New crosslinked hyaluronic compositions useful as hydrogels for controlled delivery of drugs and as tissue scaffolds.

DETAILED DESCRIPTION - A composition comprising a hyaluronic acid derivative comprising disaccharide subunits where at least 1 of the

disaccharide units has a substitution at a carboxyl group so that it is of formula (I) is new.

R', R'' = side chains containing functional groups (H, bioactive peptide, alkyl, aryl, alkylaryl; arylalkyl substituted alkylaryl containing O, N, S or P; or substituted arylalkyl containing O, N, S, P, halo or a metal atom) bound directly to each other or separated by keto, ether, amino, oxycarbonyl, sulfate, sulfoxide, carboxamide, alkyne or alkene groups. The side chain terminates with H, peptide, aldehyde, amine, arylazide, hydrazide, maleimide, sulfhydryl, optionally active ester, carboxylate, imidoester, halo or OH groups.

INDEPENDENT CLAIMS are included for:

(1) a composition comprising a **hyaluronic acid ester** of formula (II);

(2) hydrogels containing crosslinked hyaluronic acid derivatives of formulae (I) or (II);

(3) preparation of hyaluronic acid derivatives comprising:

(a) forming an activated ester on a carboxylate of a glucuronic acid group of hyaluronic acid;

(b) substituting at the carbonyl carbon of the activated ester with a side chain comprising a nucleophilic portion and a functional group portion; and

(c) optionally forming a crosslinked hydrogel from the product;

(4) forming a matrix for a temporary scaffold for tissue repair from the product of (c) above, where either:

(a) the crosslinker is a polyvalent active ester, an aldehyde, an amine, an arylazide, maleimide or sulfhydryl; or

(b) the hyaluronic acid derivative is crosslinked using transglutaminase;

(5) tissue adhesives comprising either:

(a) the hydrogel of (2) where the side chain is an activated ester, aldehyde, arylazide or maleimide;

(b) (II);

(c) a hydrogel of (2) where the crosslinked hyaluronic derivative is formed using a polyvalent active ester, aldehyde, arylazide or maleimide as cross-linker; or

(d) a hydrogel of (2) where the hydrogel is formed in the presence of growth factors, cytokines, drugs and/or bioactive peptides;

(6) matrices for cell structures comprising either:

(a) a hydrogel of (2) where either the crosslinked hyaluronic acid derivatives are formed as is (5) (c)

(b) a hydrogel as in (2) which is formed as in (5)(d);

(c) a hydrogel as in (2).

R = substituted triazole, N-sulfosuccinimide, nitrophenol, partially halogenated phenol or pentafluorophenol.

USE - The compositions are especially used for the controlled delivery of bioactive agents such as drugs, cytokines , growth factors and cells. The hydrogels are used as temporary scaffolds for tissue **regeneration** in e.g. cartilage repair. They may be used to promote bone repair, treat pathological wound conditions such as chronic ulcers, as scaffolds to generate artificial tissues or organ (e.g. skin or liver), to generate tissue separation or to prevent tissue adhesion following surgery, for tissue augmentation in plastic surgery.

ADVANTAGE - The methods allow versatile modification of hyaluronic acid allowing for crosslinking under physiological conditions, but do not compromise its molecular weight or chemical identity.

Dwg.0/13

L77 ANSWER 31 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-097079 [08] WPIDS
DOC. NO. NON-CPI: N2000-075016
DOC. NO. CPI: C2000-028131
TITLE: Biomaterials containing hyaluronic acid derivatives.
DERWENT CLASS: A11 A96 B07 D22 F07 P32 P34

INVENTOR(S): CALLEGARO, L; DONA', M; PAVESIO, A; DONA, M
PATENT ASSIGNEE(S): (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9961080	A1	19991202	(200008)*	EN	37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9943680	A	19991213	(200020)		
EP 1085917	A1	20010328	(200118)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE SI					
IT 1300254	B	20000503	(200206)		
IT 1302535	B	20000905	(200215)		
JP 2002516154	W	20020604	(200239)		42
AU 748303	B	20020530	(200247)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9961080	A1	WO 1999-EP3604	19990525
AU 9943680	A	AU 1999-43680	19990525
EP 1085917	A1	EP 1999-926410	19990525
		WO 1999-EP3604	19990525
IT 1300254	B	IT 1998-PD131	19980527
IT 1302535	B	IT 1998-PD299	19981221
JP 2002516154	W	WO 1999-EP3604	19990525
		JP 2000-550539	19990525
AU 748303	B	AU 1999-43680	19990525

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9943680	A	Based on	WO 9961080
EP 1085917	A1	Based on	WO 9961080
JP 2002516154	W	Based on	WO 9961080
AU 748303	B	Previous Publ.	AU 9943680
		Based on	WO 9961080

PRIORITY APPLN. INFO: IT 1998-PD299 19981221; IT 1998-PD131 19980527

AB WO 9961080 A UPAB: 20000215
NOVELTY - Use of hyaluronic acid derivatives is new.
DETAILED DESCRIPTION - The hyaluronic acid derivative is:
(A) an **ester** of **hyaluronic acid** in which part or all of the carboxy functions are esterified with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic alcohols;
(B) autocrosslinked **esters** of **hyaluronic acid** in which part or all of the carboxy groups are esterified with the alcoholic functions of the same polysaccharide chain or other chains;
(C) cross-linked **esters** of **hyaluronic acid** in which part or all of the carboxy groups are esterified with aliphatic, aromatic, arylaliphatic, cycloaliphatic or heterocyclic polyalcohols generating cross-linking by means of spacer chains;
(D) hemiesters of succinic acid or heavy metal salts of the hemiester

of succinic acid with hyaluronic acid or with partial or total **esters** of **hyaluronic acid**; or

(E) sulfated derivatives or N-sulfated derivatives of hyaluronic acid. The hyaluronic acid derivative is processed in the form of a three-dimensional structure enclosing empty spaces formed by communicating pores and/or fine fibers or microfibers entangled together for the preparation of a biocompatible biomaterial for the **regeneration** of mammal tissue. The biocompatible biomaterial is free from cellular components and/or products and when the hyaluronic acid derivative of from class (A) and is processed in the form of a non-woven tissue it has an esterification degree lower than 85%.

An INDEPENDENT CLAIM is included for a method for **regenerating** in vivo mammal tissue comprising application of the novel biocompatible biomaterial.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The derivatives are useful for making a biocompatible biomaterial for the **regeneration** of mammal tissue (epidermal, dermal, bone, cartilage, nerve, cardiovascular, adipose or hepatic). The derivatives are especially useful for osteochondral **regeneration**.

ADVANTAGE - The tissue obtained by the **regeneration** has the same structure and functions as natural tissue and is well integrated in the adjacent tissue cells.

Dwg.0/3

L77 ANSWER 32 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1998-557476 [47] WPIDS
DOC. NO. NON-CPI: N1998-434531
DOC. NO. CPI: C1998-166908
TITLE: Novel sulphated hyaluronic acid derivatives - useful as coatings for bio-materials such as catheters, blood bags, syringes, and surgical instruments.
DERWENT CLASS: A96 B04 D16 D22 P34
INVENTOR(S): CALLEGARO, L; RENIER, D
PATENT ASSIGNEE(S): (FIDI-N) FIDIA ADVANCED BIOPOLYMERS SRL; (FIDI-N) FIDIA ADVANCED BIOPOLYMERS
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9845335	A1	19981015	(199847)*	EN	44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9874291	A	19981030	(199911)		
EP 971961	A1	20000119	(200009)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
IT 1291444	B	19990111	(200144)		
AU 738788	B	20010927	(200170)		
JP 2001522385	W	20011113	(200204)		35
IT 1300157	B	20000503	(200205)		
US 2002037874	A1	20020328	(200225)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9845335	A1	WO 1998-EP1973	19980403

AU 9874291	A		AU 1998-74291	19980403
EP 971961	A1		EP 1998-921429	19980403
			WO 1998-EP1973	19980403
IT 1291444	B		IT 1997-PD64	19970404
AU 738788	B		AU 1998-74291	19980403
JP 2001522385	W		JP 1998-542365	19980403
			WO 1998-EP1973	19980403
IT 1300157	B		IT 1998-PD22	19980210
US 2002037874	A1	Div ex	WO 1998-EP1973	19980403
		Div ex	US 1999-402510	19991206
			US 2001-972707	20011003

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9874291	A	Based on	WO 9845335
EP 971961	A1	Based on	WO 9845335
AU 738788	B	Previous Publ.	AU 9874291
		Based on	WO 9845335
JP 2001522385	W	Based on	WO 9845335

PRIORITY APPLN. INFO: IT 1998-PD22 19980210; IT 1997-PD64 19970404

AB WO 9845335 A UPAB: 19981210
Novel sulphated hyaluronic acid derivatives (I) or their salts in which the glucosamine moieties are partially N-sulphated and optionally totally O-sulphated in position 6 are claimed.

Also claimed are: (1) a pharmaceutical composition comprising (I) or its salt in association with another pharmacologically active substance and a carrier; (2) a biomaterial comprising (I) or its salt optionally in association with a polymer and optionally further biologically active substances; (3) a biomedical object comprising a bypass, venous catheter, shunt, catheter, guide channel, probe, cardiac valve, artificial tendon, bone or cardiovascular replacement, contact lens, soft tissue replacement, replacement of animal origin, blood oxygenator, artificial kidney, heart, pancreas, liver, blood bag, syringe, surgical instrument, filtration system, laboratory instrument, container for culture or for the **regeneration** of cells or tissues or support for peptides, proteins or antibodies, coated with (I) or its salt; and (4) (I) or its salt or a mixture of (I) and optionally pharmacologically active substance, for the preparation of pharmaceutical compositions.

USE - (I) or its salt is used for treatment of inflammation, as an antiviral agent, for accelerating wound healing or burns, sores and skin ulcers, to favour angiogenesis, or for the preparation of **hyaluronic acid esters** with aliphatic, aromatic, araliphatic, cycloaliphatic or heteroaliphatic alcohol or crosslinked hyaluronic acid where part or all of the carboxy groups of D-glucuronic residue form inner esters or inter-molecular esters with the alcohol functions of the same or other polysaccharide chains (claimed). The compounds have anticoagulant and antithrombotic activities and are useful for preparation of biomaterials and coatings for biomedical objects.

ADVANTAGE - The method has reduced costs over prior art and the compounds have improved chemical physical properties over prior art.
Dwg.0/0

L77 ANSWER 33 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1997-244829 [22] WPIDS
DOC. NO. NON-CPI: N1997-201966
DOC. NO. CPI: C1997-079281
TITLE: Porous biodegradable bone grafting matrix - comprises bound network of insol. bio-polymer fibres, binder and

immobile calcium phosphate mineral and maintains structural integrity and porosity for bone replacement.

DERWENT CLASS: A96 B04 D22 P32
INVENTOR(S): KWAN, M K; PACETTI, S D; YAMAMOTO, R K
PATENT ASSIGNEE(S): (ORQU-N) ORQUEST INC; (ORQU-N) ORQUEST CORP
COUNTRY COUNT: 72
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9714376	A1	19970424	(199722)*	EN	21
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN					
AU 9675167	A	19970507	(199735)		
US 5776193	A	19980707	(199834)		
EP 855884	A1	19980805	(199835)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
AU 705303	B	19990520	(199931)		
JP 11513590	W	19991124	(200006)		17
CN 1204245	A	19990106	(200007)		
NZ 321756	A	19991129	(200031)		
US 6187047	B1	20010213	(200111)		
US 2001014830	A1	20010816	(200149)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9714376	A1		WO 1996-US16496	19961015
AU 9675167	A		AU 1996-75167	19961015
US 5776193	A	Provisional	US 1995-5523P	19951016
			US 1996-633554	19960417
EP 855884	A1		EP 1996-937686	19961015
			WO 1996-US16496	19961015
AU 705303	B		AU 1996-75167	19961015
JP 11513590	W		WO 1996-US16496	19961015
			JP 1997-515932	19961015
CN 1204245	A		CN 1996-198883	19961015
NZ 321756	A		NZ 1996-321756	19961015
			WO 1996-US16496	19961015
US 6187047	B1	Provisional	US 1995-5523P	19951016
		Div ex	US 1996-633554	19960417
			US 1998-110726	19980707
US 2001014830	A1	Provisional	US 1995-5523P	19951016
		Div ex	US 1996-633554	19960417
		Cont of	US 1998-110726	19980707
			US 2001-782794	20010213

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9675167	A	Based on	WO 9714376
EP 855884	A1	Based on	WO 9714376
AU 705303	B	Previous Publ.	AU 9675167
		Based on	WO 9714376
JP 11513590	W	Based on	WO 9714376
US 6187047	B1	Div ex	US 5776193
US 2001014830	A1	Div ex	US 5776193

Cont of US 6187047

PRIORITY APPLN. INFO: US 1996-633554 19960417; US 1995-5523P 19951016; US 1998-110726 19980707; US 2001-782794 20010213

AB WO 9714376 A UPAB: 19970530

A porous biodegradable matrix for the replacement of bone, which maintains physical integrity for at least 3 days after implant and its porosity for 7-14 days after implant into a physiological environment in which bone replacement is occurring, comprises a bound network of insoluble biopolymer fibre, binder and immobile calcium phosphate mineral.

The binder is selected from soluble collagen (preferred), gelatin, polylactic acid, polyglycolic acid, copolymers of lactic and glycolic acids, polycaprolactone, carboxymethylcellulose, cellulose **esters**, dextrose, dextran, chitosan, **hyaluronic acid**, ficol, chondroitin, sulphate, polyvinyl alcohol, polyacrylic acid, polypropylene glycol, polyethylene glycol, water soluble polyacrylates and water soluble polymethacrylates.

The biopolymer comprises fibrillar collagen.

The mineral preferably comprises hydroxyapatite, of particle diameter at least 5 mu m. It is released as particles into the physiological environment during replacement with bone in a time-release profile which maintains the physical integrity and porosity as described. The collagen and immobilised calcium phosphate are preferably in the form of mineralised collagen containing 30-80 wt.% collagen.

The matrix further may contain marrow cells, autogenous bone and one or more bone growth factors.

USE - The matrix is useful for bone repair. It can be used as a grafting material and/or as a delivery vehicle for osteogenic growth factor. It may be mixed with autogenous bone marrow and implanted for bone **regeneration**. It is particularly useful for spinal fusion, filling bone defects, fracture repair, grafting periodontal defects, maxifacial reconstruction, joint reconstruction and other orthopaedic uses.

ADVANTAGE - Structural integrity and porosity are maintained for sufficient time to augment the bone replacement process.

Dwg.0/0

L77 ANSWER 34 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1993-213836 [26] WPIDS
DOC. NO. NON-CPI: N1993-164418
DOC. NO. CPI: C1993-094839
TITLE: Biodegradable composite membrane for tissue **regeneration** - contains reinforcing mesh and matrix both of polysaccharide e.g. hyaluronic or alginic acid or ester.
DERWENT CLASS: A96 B07 D22 F04 P34
INVENTOR(S): CALLEGARO, L; DORIGATTI, F; ROMEO, A
PATENT ASSIGNEE(S): (MURS-N) MURST ITAL MIN UNIV & SCI & TECHNOLOGICA; (MURS-N) MURST; (ITUY-N) ITAL MIN UNIV RICERCA SCI & TECNOLOGICA; (ITUY-N) ITAL MIN UNIV RICERCA SCI TECNOLOGICA; (ITUY-N) ITAL MIN UNIV & SCI & TECHNOLOGICAL RES; (ITUY-N) ITAL MIN UNIV SCI & TECHNOLOGICAL RES; (MURS-N) MURST ITAL MIN UNIV & SCI & TECNOLOGICAL
COUNTRY COUNT: 41
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9311805	A1	19930624	(199326)*	EN	62
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD US					
AU 9333467	A	19930719	(199344)		
NO 9402329	A	19940817	(199436)		

```
FI 9402895    A  19940818 (199441)
EP 625056     A1 19941123 (199445)  EN
    R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
JP 07502431   W  19950316 (199519)
HU 68706      T  19950728 (199536)
IT 1254170    B  19950911 (199612)
AU 669148     B  19960530 (199629)
RO 111200     B1 19960730 (199721)
US 5622707    A  19970422 (199722)       17
EP 625056     B1 19991020 (199948)  EN
    R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69230182   E  19991125 (200002)
ES 2141145    T3 20000316 (200021)
RU 2128057    C1 19990327 (200024)
HU 217989     B  20000528 (200035)
NO 308724     B1 20001023 (200061)
CA 2126087    C  20010213 (200112)  EN
KR 252192     B1 20000601 (200130)
JP 3277212    B2 20020422 (200234)       18
PH 31415      A  19981029 (200257)#
```

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9311805	A1	WO 1992-EP2959	19921218
AU 9333467	A	AU 1993-33467	19921218
NO 9402329	A	WO 1992-EP2959	19921218
		NO 1994-2329	19940617
FI 9402895	A	WO 1992-EP2959	19921218
		FI 1994-2895	19940616
EP 625056	A1	WO 1992-EP2959	19921218
		EP 1993-902121	19921218
JP 07502431	W	WO 1992-EP2959	19921218
		JP 1993-510642	19921218
HU 68706	T	WO 1992-EP2959	19921218
		HU 1994-1838	19921218
IT 1254170	B	IT 1991-PD228	19911218
AU 669148	B	AU 1993-33467	19921218
RO 111200	B1	WO 1992-EP2959	19921218
		RO 1994-1046	19921218
US 5622707	A	US 1992-992697	19921218
EP 625056	B1	WO 1992-EP2959	19921218
		EP 1993-902121	19921218
DE 69230182	E	DE 1992-630182	19921218
		WO 1992-EP2959	19921218
		EP 1993-902121	19921218
ES 2141145	T3	EP 1993-902121	19921218
RU 2128057	C1	WO 1992-EP2959	19921218
		RU 1994-30735	19921218
HU 217989	B	WO 1992-EP2959	19921218
		HU 1994-1838	19921218
NO 308724	B1	WO 1992-EP2959	19921218
		NO 1994-2329	19940617
CA 2126087	C	CA 1992-2126087	19921218
		WO 1992-EP2959	19921218
KR 252192	B1	WO 1992-EP2959	19921218
		KR 1994-702108	19940617
JP 3277212	B2	WO 1992-EP2959	19921218
		JP 1993-510642	19921218
PH 31415	A	PH 1994-48480	19940620

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9333467	A	Based on	WO 9311805
EP 625056	A1	Based on	WO 9311805
JP 07502431	W	Based on	WO 9311805
HU 68706	T	Based on	WO 9311805
AU 669148	B	Previous Publ.	AU 9333467
		Based on	WO 9311805
RO 111200	B1	Based on	WO 9311805
EP 625056	B1	Based on	WO 9311805
DE 69230182	E	Based on	EP 625056
		Based on	WO 9311805
ES 2141145	T3	Based on	EP 625056
RU 2128057	C1	Based on	WO 9311805
HU 217989	B	Previous Publ.	HU 68706
		Based on	WO 9311805
NO 308724	B1	Previous Publ.	NO 9402329
CA 2126087	C	Based on	WO 9311805
JP 3277212	B2	Previous Publ.	JP 07502431
		Based on	WO 9311805

PRIORITY APPLN. INFO: IT 1991-PD228 19911218; PH 1994-48480 19940620

AB WO 9311805 A UPAB: 19931118

Composite membrane comprises: (A) a reinforcing mesh of at least one of hyaluronic acid (HA), alginic acid (AA) and their derivs; embedded in (B) a polymeric matrix of at least one of HA, AA and their derivs. and gelled polysaccharides (GPS).

Derivs. of HA and AA are pref. esters with pharmacologically inactive alcohols (aliphatic, araliphatic, cycloaliphatic or heterocyclic) or pharmacologically active alcohols.

GPS is pref at least one of chitin, alginate, chitosan, gellan and their (semi)synthetic derivs. Pref. both (A) and (B) are HA or derivs.; esp. (A) in the ethyl ester and (B) the benzyl or partial (esp. 75%) benzyl ester, or (A) is the benzyl ester and (B) the partial benzyl ester. Alternatively, (A) is a mixt. (pref. equal amts.) of HA benzyl ester and AA benzyl ester.

USE/ADVANTAGE - The biodegradable, biocompatible and bioabsorbable membranes are used (claimed) in surgery for the guided **regeneration** of tissues. They can be used for securing superficial and internal lesions, eg. in periodontal surgery. AH plays a role in tissue repair process, and can accelerate healing. Compared with simple HA ester membranes, the composite membranes have superior resistance to tension and tearing e.g. where suture stitches are used. The resistance and stiffness characteristics can be controlled and the two components do not separate, e.g. under wet conditions. The membranes can incorporate a wide range of drugs (e.g. antiinflammatory steroids, vitamins and (or alkaloids) in ester form

Dwg.0/3

L77 ANSWER 35 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1992-299772 [36] WPIDS
DOC. NO. NON-CPI: N1992-229582
DOC. NO. CPI: C1992-133680
TITLE: Nerve guides for **regenerating** damaged nerves - comprises hyaluronate ester matrix, hyaluronate ester reinforcement and active factor.
DERWENT CLASS: B04 D22 P34
INVENTOR(S): CALLEGARO, L; DELLA, VALLE F; ROMEO, A
PATENT ASSIGNEE(S): (FIDI-N) FIDIA SPA
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9213579	A1	19920820	(199236)*	EN	53
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE					
W: AU CA CS FI HU JP KR NO PL RU US					
AU 9211897	A	19920907	(199249)		
EP 571415	A1	19931201	(199348)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
JP 06504930	W	19940609	(199427)		12
IT 1247157	B	19941212	(199519)		
EP 571415	B1	19950719	(199533)	EN	21
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
DE 69203596	E	19950824	(199539)		
ES 2077397	T3	19951116	(199551)		
US 5735863	A	19980407	(199821)		15

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9213579	A1	WO 1992-EP285	19920210
AU 9211897	A	AU 1992-11897	19920210
		WO 1992-EP285	19920210
EP 571415	A1	EP 1992-903786	19920210
		WO 1992-EP285	19920210
JP 06504930	W	JP 1992-503965	19920210
		WO 1992-EP285	19920210
IT 1247157	B	IT 1991-PD32	19910211
EP 571415	B1	EP 1992-903786	19920210
		WO 1992-EP285	19920210
DE 69203596	E	DE 1992-603596	19920210
		EP 1992-903786	19920210
		WO 1992-EP285	19920210
ES 2077397	T3	EP 1992-903786	19920210
US 5735863	A	WO 1992-EP285	19920210
		US 1994-104025	19940524

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9211897	A	Based on	WO 9213579
EP 571415	A1	Based on	WO 9213579
JP 06504930	W	Based on	WO 9213579
EP 571415	B1	Based on	WO 9213579
DE 69203596	E	Based on	EP 571415
		Based on	WO 9213579
ES 2077397	T3	Based on	EP 571415
US 5735863	A	Based on	WO 9213579

PRIORITY APPLN. INFO: IT 1991-PD32 19910211

AB WO 9213579 A UPAB: 19931112
Medical devices for use in the treatment of damaged nerve tissue comprise: (a) a tubular matrix comprising a biocompatible, bioabsorbable, water-insoluble hyaluronate ester (I); (b) a thread or woven tube made of a biocompatible, bioabsorbable, water-insoluble hyaluronate ester (II); and (c) an active factor (III) having activity for treatment of damaged nerve tissue.

USE/ADVANTAGE - When sutured to damaged nerve stumps, the devices act as nerve guides, holding the stumps in position while (III)-promoted nerve generation takes place. Component (b) serves as a reinforcement to prevent cracking and tearing of the guide by suture threads or surgical needles

Dwg.0/0

L77 ANSWER 36 OF 36 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1991-368987 [50] WPIDS
DOC. NO. NON-CPI: N1991-282508
DOC. NO. CPI: C1991-159004
TITLE: surgical implants e.g. vascular grafts, cruciate ligament prostheses - comprise biocompatible matrix contg. microencapsulated drug(s) to provide sustained release and improve cellular uptake.
DERWENT CLASS: A96 B07 D22 P34
INVENTOR(S): JERNBERG, G R
PATENT ASSIGNEE(S): (JERN-I) JERNBERG G R
COUNTRY COUNT: 35
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9117744	A	19911128	(199150)*		
RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE					
W: AT AU BB BG BR CA CH DE DK ES FI GB HU JP KP KR LK LU MC MG MW NL NO PL RO SD SE SU					
AU 9179096	A	19911210	(199212)		
EP 528971	A1	19930303	(199309)	EN	30
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
US 5290271	A	19940301	(199409)		9
EP 528971	B1	19990901	(199940)	EN	
R: DE ES FR GB IT					
DE 69131574	E	19991007	(199947)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 528971	A1		EP 1991-910569	19910423
			WO 1991-US2784	19910423
US 5290271	A	CIP of	US 1990-523067	19900514
		Cont of	US 1990-599699	19901018
		Cont of	US 1992-899096	19920615
			US 1993-99265	19930729
EP 528971	B1		EP 1991-910569	19910423
			WO 1991-US2784	19910423
DE 69131574	E		DE 1991-631574	19910423
			EP 1991-910569	19910423
			WO 1991-US2784	19910423

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 528971	A1	Based on	WO 9117744
EP 528971	B1	Based on	WO 9117744
DE 69131574	E	Based on	EP 528971
		Based on	WO 9117744

PRIORITY APPLN. INFO: US 1990-599699 19901018; US 1990-523067 19900514; US 1992-899096 19920615; US 1993-99265 19930729

AB WO 9117744 A UPAB: 19991207
Surgical implants comprise a biocompatible matrix contg. one or more microencapsulated drugs.

The drugs are selected from (a) antibacterial agents, esp. bisbiguanides, fluorides, iodine, heavy metal salts or sulphonamides; (b)

antibiotics, esp. vancomycin, tetracycline, penicillin, cephalosporins, erythromycin, metronidazole, neomycin or kanamycin; (c) antiinflammatory agents, esp. cortisone, hydrocortisone, betamethasone, dexamethasone, prednisolone, indomethacin, flurbiprofen, meclofenamic acid, ibuprofen or naproxen; (d) anticoagulants, esp. heparin, dextran, prostacyclin or other prostaglandin analogues; and (e) tissue-**regenerating** agents, esp. fibronectin or bone morphogenic protein. The implants may also contain a carrier (esp. hyaluronic acid) capable of improving the cellular uptake of the drug. The carrier may also be microencapsulated. The matrix comprises (a) a non-resorbable material, esp. polytetrafluoroethylene (PTFE), Dacron, Proplast, polypropylene or a hyaluronic acid ether, or (b) a resorbable material, esp. crosslinked collagen or a **hyaluronic acid ester**. USE/ADVANTAGE - Specified implants include vascular grafts and cruciate ligament prostheses. The microcapsules provide sustained release of the drugs. (30pp Dwg.No.6B/7)

FILE 'HOME' ENTERED AT 13:49:39 ON 18 SEP 2002